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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/328,975	06/09/1999	JOHN A. WOLFF	MIRUS009	7574

25032 7590 03/09/2005

MIRUS CORPORATION
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EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 03/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/328,975	WOLFF ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *8* is/are allowed.

6)☐ Claim(s) *1 and 3-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 June 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

An amendment was received and entered on 12/9/04. Claims 10, 12-14, and 19 were canceled as requested.

Claims 1 and 3-8 remain pending and are under consideration in this Office Action.

Rejections Withdrawn

The rejection of claims 1 and 3-8 under 35 USC 112, second paragraph is withdrawn in view of Applicant's amendments requiring new grounds of rejection set forth below.

The rejection of claims 1, 3, 4, 5, and 7, under 35 U.S.C. 102(e) as being anticipated by Lee et al (US Patent 5,908,777) is withdrawn. The rejection was improper because the claims required addition of a charged polymer to "the complex of step a)", wherein the complex of step a) consisted of a nucleic acid and a polycation. In fact Lee taught addition of a charged polymer to a complex comprising a nucleic acid, a polycation, and anionic liposomes. The claims do not allow for this because they use closed language in referring to a complex "consisting of a nucleic acid and a polycation."

The rejection of claim 8 under 35 U.S.C. 102(a) as being anticipated by Baker et al (Gene Therapy 4:773-782, 7/31/97) is withdrawn in view of Applicant's amendment requiring that all polymers in the tertiary complex, including any polymeric nucleic acid, must comprise a block copolymer.

Specification

The amendment filed **2/8/01** is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The Examiner regrets that this objection was not raised immediately in response to the amendment. The added material which is not supported by the original disclosure is as follows.

At page 4, first paragraph of the response filed 2/8/01, Applicant reports that the term "DS" or "dextran sulfate" at specification pages 26 and 27, should be "polyacrylic acid". The specification was amended to make this change. Furthermore, although the specification as filed defined "PAA" at page 22, lines 26 and 27 as poly-L-aspartic acid, Applicant asserts that this was a mistake and that PAA should actually mean "polyacrylic acid". Amendments to this effect were made at page 27. The only support for these amendments is the assertion that the specification discloses polyacrylic acid at page 25, line 12. However, this assertion does not provide support for the substitution of "polyacrylic acid" for "dextran sulfate" and "DS" in the working example set forth at pages 26 and 27, nor does it provide support for the arbitrary redefinition of PAA as polyacrylic acid when the specification clearly applies this term to polyaspartic acid at page 22, lines 26 and 27. Applicant has provided no evidence to support that any mistake was made, and the asserted error are not obvious.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 3-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 3-7 are indefinite because they recite "the compound" in step (b) without antecedent basis.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Curiel et al (US Patent 5,547,932, issued 8/20/96) in view of Lee et al Lee et al (WO 97/00965, published 1/9/97), taken with the evidence of Dominguez (US Patent 4,049,595).

Curiel taught methods of delivering nucleic acids to cells in vivo for the purpose of expressing encoded antigens and eliciting a humoral immune response. See e.g. Brief Summary paragraph 4. In one method a ternary complex is formed by combining a DNA with an amount of a polylysine-galactose ligand conjugate sufficient to neutralize

half of the DNA negative charge. The remainder of the charger is used to load a charged polylysine-influenza virus hemagglutinin HA-2 peptide.

Curiel is silent as to the net charge of the resulting complex.

Lee taught that targeted cationic nucleic acid delivery complexes allow non-specific, non-targeted cellular uptake due to the fact that cells generally have a negative surface charge. Despite the presence of a targeting ligand, the charge attraction between positively charged complexes and negatively charged cells leads to non-specific interactions and uptake. Lee taught that this problem could be avoided by rendering targeted delivery complexes negative in net charge. See page 2, lines 11-16, and page 9, lines 18-25.

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the invention of Curiel by loading an amount of polylysine-influenza virus hemagglutinin HA-2 peptide conjugate such that the resulting complex carried a net negative charge. One would have been motivated to do so in order to minimize non-specific uptake by cells and to thereby take maximum advantage of the galactose targeting ligand.

Inclusion of claim 6 in this rejection depends on the definition of the claim term "block copolymer". The instant specification does not define this term, so it has been given its broadest reasonable interpretation. It is apparent from the disclosure of Dominguez (US Patent 4,049,595) that "block copolymer" can be reasonably interpreted as a generic term embracing the subgenus of graft copolymers. For example, Dominguez states in the first paragraph of the detailed description:

The block copolymers employed in the present composition are thermoplastic elastomers and have at least two monoalkenyl arene polymer end blocks A and at least one elastomeric conjugated diene polymer mid block B. The number of blocks in the block copolymer is not of special importance and the macromolecular configuration may be linear, graft or radial (branched) depending upon the method by which the block copolymer is formed.

Accordingly the phrase "block copolymer" would embrace any polymer comprising at least two distinguishable blocks, regardless of linear, graft, or radial architecture.

The polylysine conjugates of Curiel taught are considered to be graft copolymers because they each comprise a peptide grafted to polylysine. One copolymer consisted of polylysine (average chain length 290) grafted with a positively charged, branched, galactosylated peptide: Lys-(N_{ε}-Lys)Lys-Gly-Ser-Gly-Gly-Ser-Gly-Gly-Ser-Gly-Gly-Cys. See column 43, line 24 to column 25, line 11. This represents the polycation of the instant claims. The other copolymer consisted of polylysine (chain length 300) grafted with an anionic peptide derived from the influenza virus hemagglutinin HA subunit: Gly-Leu-Phe-Glu-Ala-Ile-Ala-Gly-Phe-Ile-Glu-Asn-Gly-Trp-Glu-Gly-Met-Ile-Asp-Gly-Gly-Gly-Cys. This represents the charged polymer of the instant claims.

Thus the invention as a whole was prima facie obvious.

Conclusion

Claim 8 is allowable, however it is suggested that Applicant should amend the phrase "each polymer" in part c) to read --the polyanion and the polycation polymers--. As written, the claim could be interpreted as requiring that the nucleic acid, which may be a polymer, must also be a block copolymer.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-

272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, John Leguyader, be reached at 571-272-0760. The official central fax number is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Richard Schnizer, Ph.D.

S #	Updt	Database	Query	Time	Comn
S16532	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	complex and anionic polymer and (polymer same anion$) and nucleic and (polycation$ or polylysine or poly l lysine or poly lysine or polyethyleneimine or pll or pei)	2005-03-02 12:15:11	
S16531	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	anionic polymer and (polymer same anion$) and nucleic and (polycation$ or polylysine or poly l lysine or poly lysine or polyethyleneimine or pll or pei)	2005-03-02 12:15:09	
S16530	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(polymer same anion$) and nucleic and (polycation$ or polylysine or poly l lysine or poly lysine or polyethyleneimine or pll or pei)	2005-03-02 12:14:42	

S16529	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(lee and huang).in. and (anion$ or negative$) and liposome	2005-03-02 07:20:03
S16528	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	huang.in. and (lee or gao).in. and (anion$ or negative$) and net negative	2005-03-02 07:17:07
S16527	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	huang.in. and (lee or gao).in. and (anion$ or negative$) and polycation and net negative	2005-03-02 07:16:33
S16526	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	huang.in. and (lee or gao).in. and (anion$ or negative$) and polycation	2005-03-02 07:14:58
S16525	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(reticuloendothelial or reticulo-endothelial) and (negative$ same charge$) and polycation$ and (target$ same ligand) and ((reticuloendothelial or reticulo-endothelial) same clear$4)	2005-03-02 07:09:07
S16524	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(reticuloendothelial or reticulo-endothelial) and (negative$ same charge$) and polycation$ and (target$ same ligand)	2005-03-02 07:08:02
S16523	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(reticuloendothelial or reticulo-endothelial) and	2005-03-02 07:07:35

			(negative$ same charge$) and polycation$	
S16522	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(reticuloendothelial or reticulo-endothelial) and (negative$ same charge$)	2005-03-02 07:07:12
S16521	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	5547932.pn. and hemagglutinin	2005-03-02 06:45:42
S16520	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	5547932.pn. and lactosylated peptide	2005-03-02 06:38:46
S16519	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	4,049,595.pn.	2005-03-02 06:27:11
S16518	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(gao and huang).in. and polylysine	2005-03-01 14:44:09
S16517	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(gao and huang).in.	2005-03-01 14:43:52
S16516	U	USPT	5547932.pn. and antigen$	2005-03-01 14:31:09
S16515	U	USPT	5547932.pn. and immun$	2005-03-01 14:29:12
S16514	U	USPT	5547932.pn. and influenza peptide-polylysine conjugate	2005-03-01 14:04:53
S16513	U	USPT	5547932.pn.	2005-03-01 13:58:35
S16512	U	USPT	5981273.pn. and (influenza same SEQ)	2005-03-01 13:52:34
S16511	U	USPT	5981273.pn. and influenza	2005-03-01

				13:50:44
S16510	U	USPT	5981273.pn.	2005-03-01 13:50:07
S16509	U	USPT	birnstiel.in. and protamine and charge$	2005-03-01 13:21:57
S16508	U	USPT	birnstiel.in. and protamine and (net charge or surface charge)	2005-03-01 13:21:35
S16507	U	USPT	birnstiel.in. and protamine	2005-03-01 13:20:13
S16506	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	birnstiel.in. and protamine	2005-03-01 13:18:53
S16505	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	birnsteil.in. and protamine	2005-03-01 13:18:41
S16504	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	5789230.pn.	2005-03-01 13:16:49
S16503	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(nucleic or polynucle$ or vector or gene or oligonucle$) and (polycation$ or polylysine or polyethyleneimine or polyethylenimine) same dropwise and (net negative same complex)	2005-03-01 13:11:45
S16502	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	6265387.pn.	2005-03-01 13:02:00
S16501	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	dropwise and ((polycation$ or polylysine or polyethyleneimine	2005-03-01 12:50:32

			or polyethylenimine) same (nucleic or polynucle$ or vector or gene or oligonucle$)) and (net negative same complex)	
S16500	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	((polycation$ or polylysine or polyethyleneimine or polyethylenimine) same (nucleic or polynucle$ or vector or gene or oligonucle$)) and (net negative same complex)	2005-03-01 12:50:20
S16499	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	dropwise and ((polycation$ or polylysine or polyethyleneimine or polyethylenimine) same (nucleic or polynucle$ or vector or gene or oligonucle$)) and net negative	2005-03-01 12:49:55
S16498	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	((polycation$ or polylysine or polyethyleneimine or polyethylenimine) same (nucleic or polynucle$ or vector or gene or oligonucle$)) and net negative	2005-03-01 12:49:28
S16497	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(nucleic or polynucle$ or vector or gene or	2005-03-01 12:47:02

			oligonucle$) and (polycation$ or polylysine or polyethyleneimine or polyethylenimine) same dropwise and (negativ$ or anion$) and net negative	
S16496	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(nucleic or polynucle$ or vector or gene or oligonucle$) and (polycation$ or polylysine or polyethyleneimine or polyethylenimine) same dropwise and (negativ$ or anion$)	2005-03-01 12:43:21
S16495	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(nucleic or polynucle$ or vector or gene or oligonucle$) and (polycation$ or polylysine or polyethyleneimine or polyethylenimine) same dropwise and (negativ$ or anion$)	2005-03-01 11:49:53
S16494	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(nucleic or polynucle$ or vector or gene or oligonucle$) and (polycation$ or polylysine or polyethyleneimine or polyethylenimine)	2005-03-01 11:49:25

				same dropwise	
S16493	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(polycation$ or polylysine or polyethyleneimine or polyethylenimine) same dropwise		2005-03-01 11:48:52